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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,721	10/26/2001	Naohiro Terada	5853-207	9675

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
07/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/045,721	TERADA ET AL.	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,6 and 14-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 5, 6, and 14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/10/07 has been entered.

Claims 1, 3, 5, 6, and 14-20 are presently pending and considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5, 6, and 14-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "a first test substance and … a second test substance" in step (D). It is unclear if this is the first test substance and the second test substance of step (A) or if this is another two test substances. Further, if it is a new test substance, it is unclear what the first and second test substances of step (A) are used for.

Claims 3, 5, 6, and 14-20 are rejected for depending from rejected base claim and not overcoming the clarity issues of such base claim.

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5, 6, and 14-20 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, from which all the other pending claims are dependent, and therefore encompass, encompasses a method for identifying any drug candidate for promoting tissue-specific differentiation of an embryonic stem cell into any type of cell, with specific method steps comprising a pre-culturing step for two days (step B) and a culturing step of at least about 5 days on a collagen coated culture plate (step c). Claims 3, 5, 6, and 14-20 are also rejected, as they do not modify the method in such a manner to allow possession, for the reasoning below.

Applicant only broadly avers that support for this amendment is present in the specification, without further explanation of how the originally-filed specification and claims provide support for such a broad limitation. (Applicant is reminded that it is their responsibility to demonstrate support, and not the Examiner's duty to fish out support for the claims.)

The Examiner has reviewed the specification, and found that no explicit support for such a limitation exists, e.g., pp. 1-2, which provide the most explicit support for the claims, does not teach culturing prior to addition of test substances for any specific time period, nor does it teach

the use of collagen coated plates. Moreover, such indicates that the culturing of step C is performed under conditions which promote tissue-specific differentiation, but not collagen.

Hence, the specification provides no explicit support for the limitation. However, page 13 of the specification (paragraph 3), uses implicit disclosure of a specific experiment to show that EB bodies may differentiated from mouse ES cells after two days in hanging drop culture, and then performs 3 additional days in suspension culture, followed by more specific steps to be further differentiated under specific conditions into **hepatocytes** (pp. 13-16). Moreover, Applicant's equivalent to test substances were subsequently added, which are limited to specific factors (p. 16, paragraph 2), and further indicates that the collagen promotes tissue specific differentiation into hepatocytes (p. 16, paragraph 3).

Hence, at best, Applicant's disclosure relies on obviousness to produce the generic test method, and obviousness at the time of invention does not substitute for possession of the invention by Applicant at the time of invention.

Therefore, the Artisan could not determine that Applicant was in possession of a generic method to identify drug candidates for promoting tissue-specific differention of an ES cell, comprising the method claimed, except that method, limited to the steps and materials disclosed, as in page 13 of the specification, and which would further determine Applicant's disclosure to indicate that only heptocyte lineage cells were possessed.

Response to Argument – new matter

Applicant's argument 5/10/07 has been fully considered but is not found persuasive.

Applicant quotes case law and describes to the Examiner various aspects of determination of possession, and broadly avers that the written description requirement is met (p. 8).

Such is not persuasive. Applicant has failed to identify which aspects of the Examiner's analysis are incorrect, and the Examiner fails to find how his analysis is incorrect. Hence, the rejection is maintained.

Claim Rejections - 35 USC § 112 - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5-6, and 14-20 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the identification of substances which cause EBs to differentiate into the hepatic lineage, does not reasonably provide enablement for a method to screen for substances which cause differentiation into any lineage from EBs, or any tissue specific lineage from ES cells, for reasons of record, as elaborated upon below. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

As it appears that Applicant is preparing for an appeal, the rejection has been elaborated upon for the board's possible review in the future.

Applicant's claims are drawn to identifying compounds that cause ES cells to differentiate into any specific tissues, however, the cells are cultured for at least about 5 days prior to adding the test substances.

The specification teaches that the steps of the method are only for forming hepatocytes from EB bodies (EXAMPLE 2). Further, the specification states that the culturing on collagen coated plates further induces differentiation into hepatocytes (p. 16, paragraph 3).

The Art of record fails to demonstrate that the breadth of any cell type could be formed under such protocols, and because the collagen at step (C) appears to induce differentiation into heptocytes, the Artisan could not reasonably predict any other cell type could be formed, as the collagen may overpower any other differentiation pathway. While the Art demonstrates many cell types being formed from ES cells, each appears in the Art to have distinct culturing conditions (e.g., Verfaillie, et al. (2002) Hematology, 1: 369-91, pages 378-80), and whether or not this reflects a pluripotent potential for all lineages of embryonic stem cells or whether it reflects something remains to be determined (e.g., Anderson, et al. (2001) Nature Medicine, 7(4): 393-95, whole article). Essentially what these articles demonstrate is that depending on culture conditions, embryonic stem cells can differentiate into a population that gives rise to various particular lineages of cells (e.g., Verfaillie, p. 379, col. 1, paragraph 2). This is from the classic view of developmental processes, wherein cells differentiate through a complex set of branches, producing various intermediate differentiated cells, which are not quite fully differentiated, down to, at the terminus of multiple differentiations, a specific differentiated somatic cell type (e.g., Anderson, p. 393, col. 1, paragraph 3). However, from the confluence of these articles, it appears unclear whether a cell, depending on its differentiation status (i.e., how far down the tree of differentiation toward a specific phenotype) such cell can differentiate into any other specific differentiated cell type, even if not within the "tree" of differenitiation such cell has already commited to, or whether all cells, until fully differentiated, can form any other specific cell type,

or whether such cells can form a subset of those differentiated cell types not within the tree of differentiation, as well as those cell types within such tree of differentiation (e.g., Anderson, p. 393). This is further compounded in the Artisan's mind by the requirement for collagen, which induces differentiation toward a specific cell type in Applicant's specification, and may therefore, not "allow" differentiation into other cell types unless the collagen were removed.

Still further, the Art demonstrates that specific cell lineages may not be able to be formed, unless the matrix upon which they are cultured is changed (e.g., Maldonado, et al. (2000) Pancreas, 21(1): 93-96, ABSTRACT), as the matrix has a critical influence on the differentiation pathways.

Therefore, the Artisan would not reasonably predict that a culture condition comprising the collagen, which, as shown by Applicant, induces differentiation toward hepatocytes, would necessarily produce any other specific type of cell.

Hence, the Artisan would have to experiment to determine if any specific obtained compound can actually cause differentiation of an ES cell into any specific cell type other than hepatocytes.

Such experimentation is considered undue amounting to inventing Applicant's screen for its breadth for Applicant.

Response to Argument – Enablement

Applicant's argument of 5/10/07 has been fully considered but is not found persuasive.

Applicant argues indirectly, quoting case law, that because they demonstrate differentiation into hepatocytes, such bears a reasonable correlation to the broad genera of any tissue of the body, and therefore, they are enabled for the breadth of any tissue (p. 6).

Such is not persuasive. Applicant has already stated that collagen induces differentiation toward the hepatocyte lineage (p. 16, paragraph 3, as noted above, and in the record), and therefore, the Artisan would not reasonably predict that any particular tissue other than hepatocytes could be made.

Applicant argues that a patent need not teach, but preferably omits what is well known in the Art, and the Artisan could perform the method without undue experimentation for any specific cell type, and given their showing of a particular differentiation, the claims are enabled for their breadth (pp. 6-7).

The Examiner does not argue that ES cells could form a well known array of cell types, but that the Art demonstrates that it is not reasonably predictable, given the at least partial differentiation induced by collagen, that any other cell could be produced by the method, except that of hepatocytes. Hence, it would appear the argument implied by Applicant does not apply in this case, as the unpredictability is due to the lack of predictability that a commited cell type of any specific lineage could produce a commited cell type of any other specific lineage, for its breadth, and not that any specific lineage could be formed from ES cells. Moreover, the Art completely omits discussion of the influence of collagen, and as such, Applicant has not left anything out of the specification with regard to such aspect.

Such is not persuasive.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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